Figure 1

DESIGN OF CDR-GRAFTED ANTI-RSV F PROTEIN VH

```
                    5                   10                  15                  20
Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val   Human HV3 VH

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala Ser Val Lys Val   "CDR Grafted" VH
 *               *                       *   *   *               *           *
Glu Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ala Leu Val Lys Leu   Murine 1308F VH

                    25                  30                  35                  40
Ser Cys Lys Ala Ser Gly Tyr Thr Phe Asn Ser Tyr Tyr Met His Trp Val Arg Gln Ala
                         *   *   *   *   *           *   *
Ser Cys Lys Ala Ser Gly Phe Asn Ile Lys Asp Tyr Tyr Ile Tyr Trp Val Arg Gln Ala
                                        CDR 1                           *       *
Ser Cys Lys Ala Ser Gly Phe Asn Ile Lys Asp Tyr Tyr Ile Tyr Trp Val Lys Gln Arg

                    45                  50                  55                  60
Pro Gly Gln Gly Leu Glu Trp Met Gly Ile Ile Asn Pro Ser Gly Gly Ser Thr Ser Tyr
                             *       *       *       *   *       *       *   *
Pro Gly Gln Gly Leu Glu Trp Ile Gly Trp Ile Asp Pro Glu Asn Gly Asn Thr Val Phe
     *                                      CDR 2
Pro Glu Gln Gly Leu Glu Trp Ile Gly Trp Ile Asp Pro Glu Asn Gly Asn Thr Val Phe

                    65                  70                  75                  80
Ala Gln Lys Phe Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Ser Thr Val Tyr
     *
Asp Pro Lys Phe Gln Gly Arg Val Thr Met Thr Arg Asp Thr Ser Thr Ser Thr Val Tyr
                         *   *   *   *       *               *   *       *
Asp Pro Lys Phe Gln Gly Lys Ala Ser Ile Thr Ser Asp Thr Ser Ser Asn Thr Ala Tyr

                    85                  90                  95                  100
Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala

Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Tyr Tyr Gly
                         *
Leu Gln Leu Ser Ser Leu Thr Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Tyr Tyr Gly
                                                                <<V  /    D
                105                 110                 115
 -   -   -   -   -   -   -   -   -   -   -   -   -   -   -   -   -

Thr Ser Ser Phe Asp Phe Trp Gly Gln Gly Thr Thr Leu Thr Val Ser Ser
        CDR 3
Thr Ser Ser Phe Asp Phe Trp Gly Gln Gly Thr Thr Leu Thr Val Ser Ser
           /  J>>
```

In the "CDR Grafted" VH rows, the CDR stretches are underlined: Asp Tyr Tyr Ile Tyr (CDR 1), Trp Ile Gly Trp Ile Asp Pro Glu Asn Gly Asn Thr Val Phe (CDR 2), Tyr Tyr Gly … Thr Ser Ser Phe Asp Phe (CDR 3). Also underlined: Arg Val Thr Met Thr Arg Asp Thr Ser Thr Ser Thr Val Tyr in the Human HV3 VH row (positions 67–80), and Asp Pro Lys Phe Gln Gly in the Murine 1308F VH row (positions 61–66).

Figure 2

DESIGN OF CDR-GRAFTED ANTI-RSV F PROTEIN VL

```
                    5                   10                  15                  20
Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly Asp Arg Val Thr  - Human K102 VL

Asp Il  Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val Gly Asp Arg Val Thr  - "CDR Grafted" VL
        *                       *   *   *   *       *       *
Asp Ile Lys Met Thr Gln Ser Pro Ser Ser Met Tyr Val Ser Leu Gly Glu Arg Val Thr  - Murine 1308F VL

                   25                  30                  35                  40
Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser Ser Trp Leu Ala Trp Tyr Gln Gln Lys Pro
             *           *       *   *   *       *
Ile Thr Cys Lys Ala Ser Gln Asp Ile Asn Arg Tyr Leu Asn Trp Tyr Gln Gln Lys Pro
                                 CDR 1                              *
Ile Thr Cys Lys Ala Ser Gln Asp Ile Asn Arg Tyr Leu Asn Trp Phe Gln Gln Lys Pro


                   45                  50                  55                  60
Gly Lys Ala Pro Lys Leu Leu Ile Tyr Asp Ala Ser Ser Leu Glu Ser Gly Val Pro Ser
                                    *       *   *       *   *
Gly Lys Ala Pro Lys Leu Leu Ile Tyr Arg Ala Asn Arg Leu Val Asp Gly Val Pro Ser
          *           *           *                 CDR 2
Gly Lys Ser Pro Lys Thr Leu Ile His Arg Ala Asn Arg Leu Val Asp Gly Val Pro Ser


                   65                  70                  75                  80
Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
                                    *       *   *                           *
Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
                                    *       *   *
Arg Phe Ser Gly Ser Gly Ser Gly Gln Glu Tyr Ser Leu Thr Ile Ser Ser Leu Glu Phe


                   85                  90                  95                 100
Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Tyr Asn Ser Tyr Ser  -   -   -
                                    *       *   *   *   *
Asp Asp Phe Ala Thr Tyr Tyr Cys Leu Gln Phe His Glu Phe Pro Tyr Thr Phe Gly Gly
 *       *   *   *                              CDR 3
Glu Asp Met Gly Ile Tyr Tyr Cys Leu Gln Phe His Glu Phe Pro Tyr Thr Phe Gly Gly
                                                        <<V  /  J>>

                  105
 -   -   -   -   -   -   -

Gly Thr Lys Leu Glu Ile Lys

Gly Thr Lys Leu Glu Ile Lys
```

5' gcgaattccatggactggacctggagggtc 3'

MetAspTrpThrTrpArgValPheCysLeuLeuAlaValAlaProGlyAlaHisSerGln

5' [redacted] 62

1---------+---------+---------+---------+---------+---------+

3' TACCTGACCTGGACCTCCCAGAAGACGAACGACCGACATCGTGGTCCACGGGTGAGGGTC

ValGlnLeuValGlnSerGlyAlaGluValLysLysProGlyAlaSerValLysValSer

[redacted]TTTCC

61---------+---------+---------+---------+---------+---------+

CACGTCGACCACGTCAGACCTCGACTC[redacted]

CysLysAlaSerGlyPheAsnIleLysAspTyrTyrIleTyrTrpValArgGlnAlaPro

TGCAAGGCATCTGGATTCAACATTAAGGACTACTACATTTACTGGGTGCGACAGGCTCCT

121---------+---------+---------+---------+---------+---------+

[redacted]

GlyGlnGlyLeuGluTrpMetGlyTrpIleAspProGluAsnGlyAsnThrValPheAsp

GGACAA[redacted]

181---------+---------+---------+---------+---------+---------+

[redacted]TAACTGGGACTCTTACCATTATGACACAAACTG

ProLysPheGlnGlyArgValThrMetThrArgAspThrSerThrSerThrValTyrMet

CCGAAGTTCCAGGGCAGAGTCACCATGACCAGGGACACGTCCACGAGCACAGTCTACATG

241---------+---------+---------+---------+---------+---------+

GGCTTCAAGGTCCCGTCTCAGTGGTACTGGTCCCTGTGCA[redacted]

GluLeuSerSerLeuArgSerGluAspThrAlaValTyrTyrCysAlaTyrTyrGlyThr

GAGCTGAGCAGCCTGAGATCTGAGGACACGGCCGTGTATTACTGTGCGTACTACGGTACA

301---------+---------+---------+---------+---------+---------+

[redacted]

SerSerPheAspPheTrpGlyGlnGlyThrThrLeuThrValSerSer

AGCTCCTTTGACTTCTGGGGCCAAGGCACCACTCTCACAGTGAGCTCA

361---------+---------+---------+---------+--------

[redacted]GTTCCGTGGTGAGAGTGTCACTCGAGTattcctagg 5'

3' ggtgagagtgtcactcgagtattcctagggc 5'

Figure 3. oligo's used to make Hu1308 VH

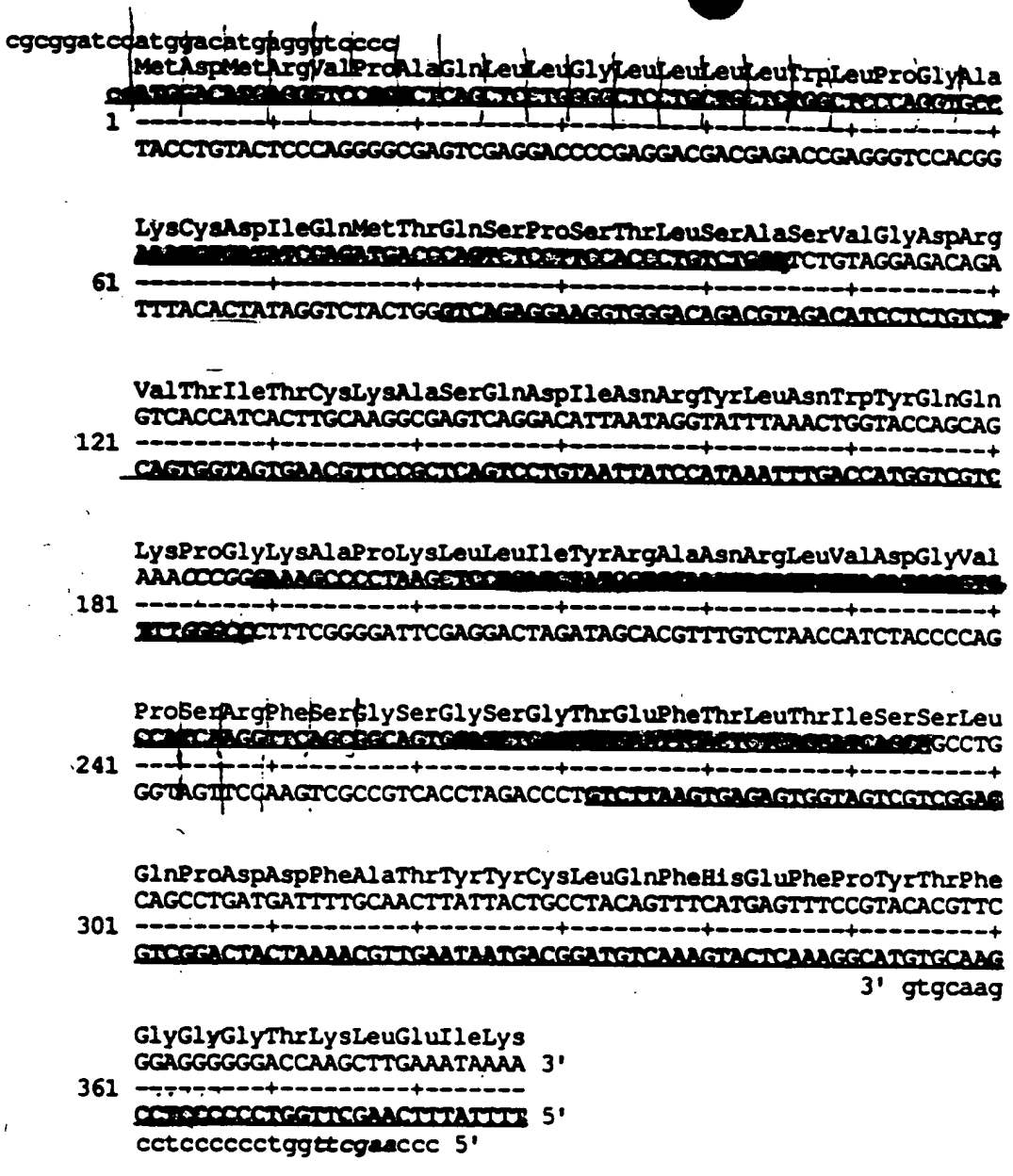

Figure 4. Oligos used to make Hu308 V_L

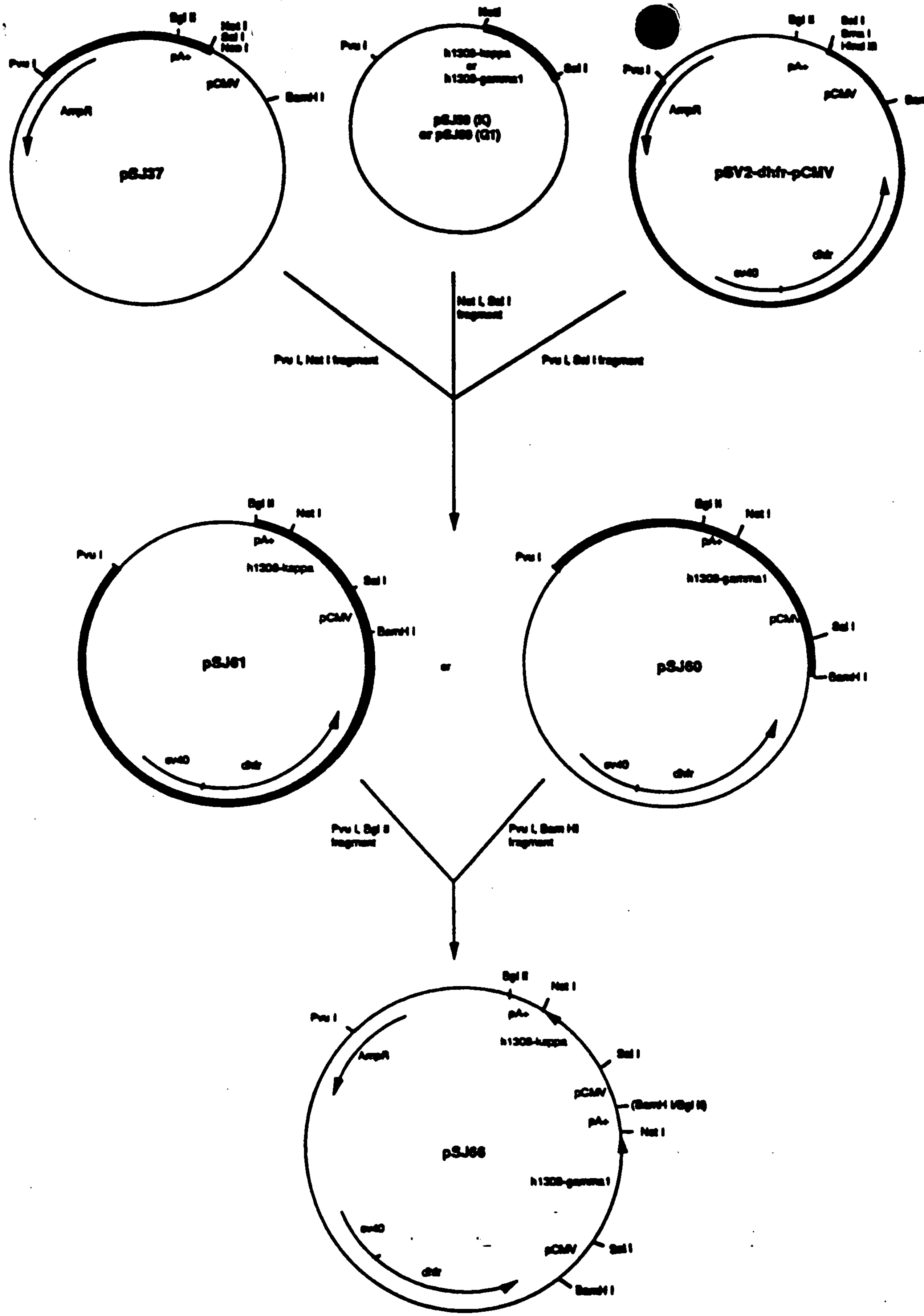

Fig 5. Construction of ~~??~~ Humanized 1308 expression vectors

Neutralizati n of RSV

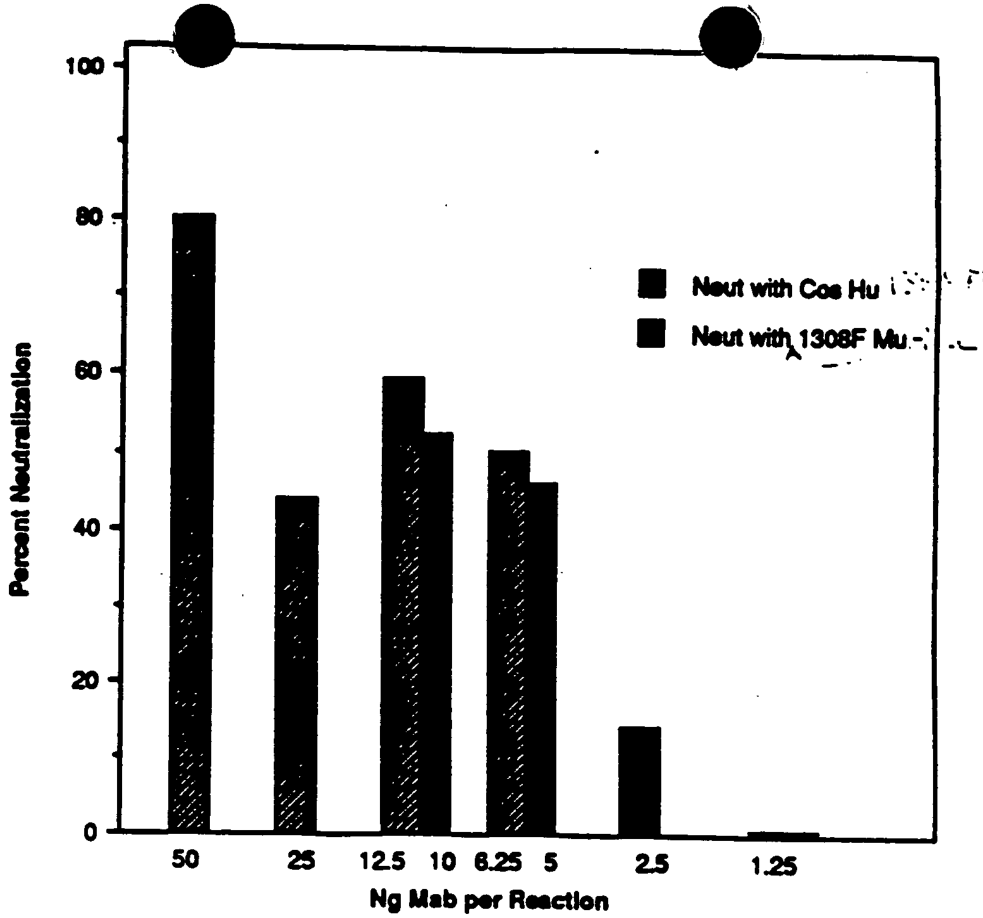

FIGURE 6

Design of Humanized VH f r anti-RSV Mab 1129

```
                5                  10                  15
    Gln Val Thr Leu Arg Glu Ser Gly Pro Ala Leu Val Lys Pro Ser  Human VH (Cor)
1   Gln Val Thr Leu Arg Glu Ser Gly Pro Ala Leu Val Lys Pro (Ser) "Humanized" VH
    Gln Val Glu Leu Gln Glu Ser Gly Pro Gly Ile Leu Gln Pro Ser  Murine 1129 VH

    Gln Thr Leu Thr Leu Thr Cys Ser Phe Ser Gly Phe Ser Leu Ser
16  Gln Thr Leu Thr Leu Thr Cys (Ser) Phe Ser Gly Phe Ser Leu Ser
    Gln Thr Leu Ser Leu Thr Cys Ser Phe Ser Gly Phe Ser Leu Ser

    Ser Ser Gly Met Cys Val Gly Trp Ile Arg Gln Pro Pro Gly Lys
31  Thr Ser Gly Met Ser Val Gly Trp Ile Arg Gln Pro Pro Gly Lys
    Thr Ser Gly Met Ser Val Gly Trp Ile Arg Gln Pro Ser Gly Glu

    Ala Leu Glu Trp Leu Ala Asp Ile Glu Trp Asp Asp Asp Lys Asp
46  Ala Leu Glu Trp Leu Ala Asp Ile Trp Trp Asp Asp Lys Lys Asp
    Gly Leu Glu Trp Leu Ala Asp Ile Trp Trp Asp Asp Lys Lys Asp

    Tyr Asn Thr Ser Leu Asp Thr Arg Leu Thr Ile Ser Lys Asp Thr
61  Tyr Asn Pro Ser Leu Lys Ser Arg Leu Thr Ile Ser Lys Asp Thr
    Tyr Asn Pro Ser Leu Lys Ser Arg Leu Thr Ile Ser Lys Asp Thr

    Ser Lys Asn Gln Val Val Leu Thr Val Thr Asn Val Asp Pro Ala
76  Ser Lys Asn Gln Val Val Leu Lys Val Thr Asn (Val) Asp Pro Ala
    Ser Ser Asn Gln Val Phe Leu Lys Ile Thr Gly Val Asp Thr Ala

    Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Ile Thr Val Ile Pro Ala Pro Ala Gly
91  Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Ser Met Ile Thr Asn Trp  -   -   -
    Asp Thr Ala Thr Tyr Tyr Cys Ala Arg Ser Met Ile Thr Asn Trp  -   -   -

    Tyr Met Asp Val Trp Gly Arg Gly Thr Pro Val Thr Val Ser Ser
106 Tyr Phe Asp Val Trp Gly Ala Gly Thr Thr Val Thr Val Ser Ser
    Tyr Phe Asp Val Trp Gly Ala Gly Thr Thr Val Thr Val Ser Ser
```

Figure 7

DESIGN OF CDR-[redacted]TED ANTI-RSV MAb 1129 V_L

```
                5                  10                  15
Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val   - Human K102 VL
Asp Ile Gln Met Thr Gln Ser Pro Ser Thr Leu Ser Ala Ser Val   - "CDR Grafted" VL
Asp Ile Gln Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Pro   - Murine 1129 VL

               20                  25                  30
Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Ser Ile Ser
Gly Asp Arg Val Thr Ile Thr Cys Lys Cys Gln Leu Ser Val Gly
                                                  CDR 1
Gly Glu Lys Val Thr Met Thr Cys Ser Ala Ser Ser Ser Val Gly

               35                  40                  45
Ser Trp Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys
Tyr Met His   - Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys
Tyr Met His   - Trp Tyr Gln Gln Lys Ser Ser Thr Ser Pro Lys

               50                  55                  60
Leu Leu Ile Tyr Asp Ala Ser Ser Leu Glu Ser Gly Val Pro Ser
Leu Trp Ile Tyr Asp Thr Ser Lys Leu Ala Ser Gly Val Pro Ser
                          CDR 2
Leu Trp Ile Tyr Asp Thr Ser Lys Leu Ala Ser Gly Val Pro Gly

               65                  70                  75
Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile
Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile
Arg Phe Ser Gly Ser Gly Ser Gly Asn Ser Tyr Ser Leu Thr Ile

               80                  85                  90
Ser Ser Leu Gln Pro Asp Asp Phe Ala Thr Tyr Tyr Cys Gln Gln
Ser Ser Leu Gln Pro Asp Asp Phe Ala Thr Tyr Tyr Cys Phe Gln
Ser Ser Ile Gln Ala Glu Asp Val Ala Thr Tyr Tyr Cys Phe Gln

               95                 100                 105
Tyr Asn Ser Tyr Ser
Gly Ser Gly Tyr Pro Phe Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
      CDR 3
Gly Ser Gly Tyr Pro Phe Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys
```

<<V / J>>

Figure 8

Oligonucleotides for th construction of the Humanized 1129 VH gene segment

Figure 9

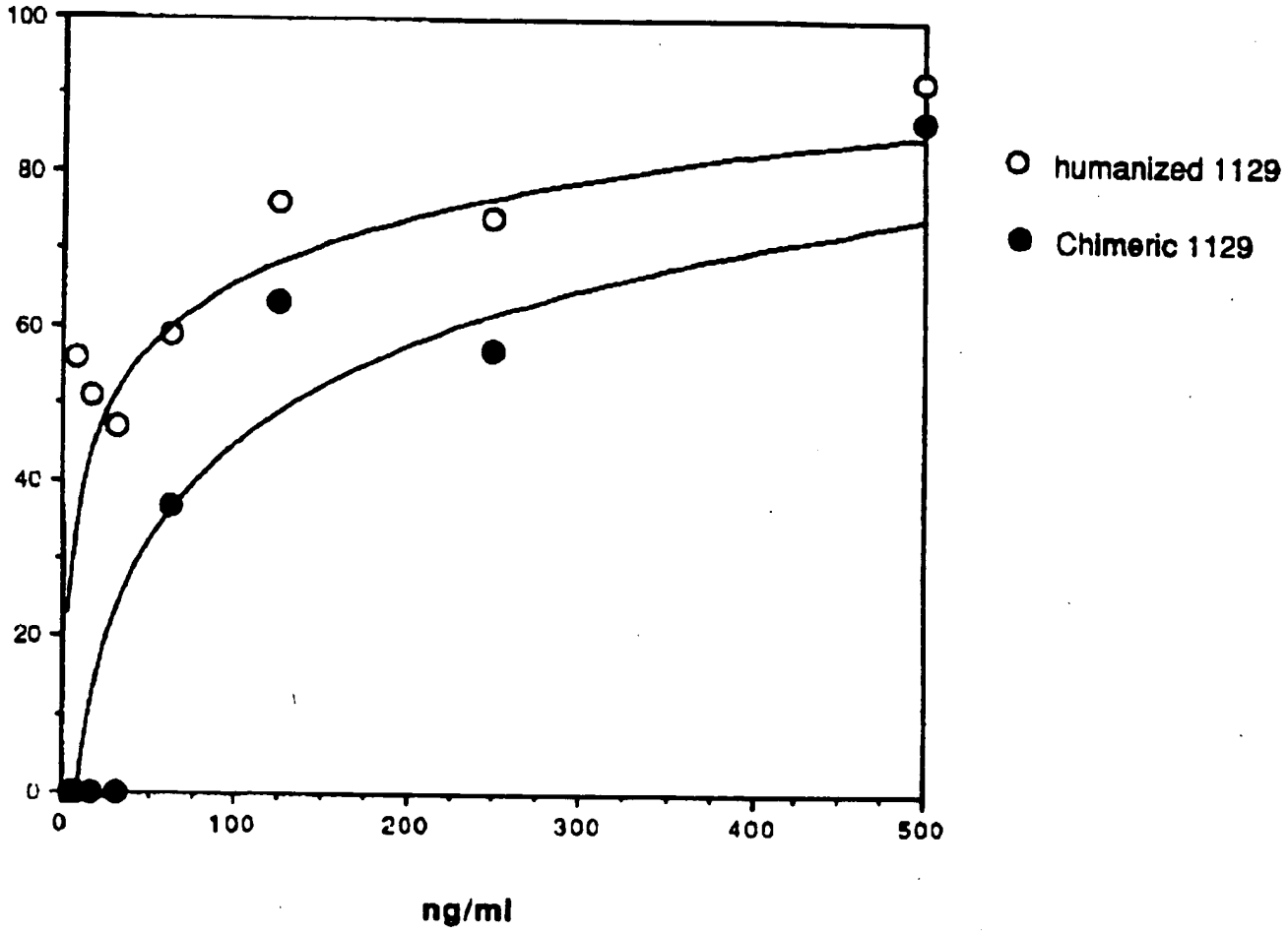
100
80
60
40
20
0
% Neutralizati n
0
100
200
300
400
500
ng/ml
humanized 1129
Chimeric 1129

Figure 10